

Dissociation Temperatures of Urea Complexes of Long-Chain Fatty Acids, Esters, and Alcohols

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A New Characterization Technique

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The literature on identification of long-chain fatty acids, esters, and alcohols is relatively sparse. In addition, numerous difficulties arise in attempting to utilize chemical derivatives for identification purposes. Urea complexes have been prepared in high yield from 42 long-chain compounds, consisting of fatty acids, methyl and vinyl esters, alcohols, a mono- and diglyceride, and a vinyl ether. These include several *cis-trans* pairs (oleic-elaidic acids, methyl oleate-elaidate, oleyl-elaidyl alcohols) and some long-chain compounds with oxygen-containing functional groups (oxirane, hydroxyl, keto) in the chain. With a few exceptions, the dissociation temperature of each of these complexes has been determined. At this temperature, the complex dissociates and the transparent hexagonal crystals are converted to an opaque mass of microcrystals. The dissociation temperature, which is the temperature at which

opacity first occurs when a transparent crystal of a urea complex is slowly heated, is characteristic for each complex and can be readily duplicated ($\pm 1.5^\circ$). Urea complexes meet almost all the criteria for an ideal derivative. The dissociation temperatures of adjacent or closely adjacent members of the four homologous series studied (fatty acids, methyl esters, alcohols, and vinyl esters) are sufficiently far apart to permit this new characteristic to be employed for identification purposes. The technique can be used on a semimicro or micro scale, and the organic compound bound in the complex can be readily recovered. The crystals of complex are large and readily handled, the weight of complex obtained is usually three to four times that of the organic compound being treated with urea, no special reagents are required, and "crude" complexes are usually analytically pure without recrystallization.

THE usual schemes for the positive identification of organic compounds include the preparation of suitable solid chemical derivatives (3, 7, 11, 20). The literature on identification of the long-chain fatty acids, esters, and alcohols reveals numerous difficulties in attempting to utilize derivatives for this purpose. For example, although many derivatives of long-chain fatty acids have been reported, the melting points of specific derivatives (amide, *p*-bromoanilide, *p*-phenylphenacyl ester, etc.) of many members of this homologous series are usually too close together to permit positive identification. Derivatives of long-chain alcohols suffer from the same drawback and, in addition, the literature on them is relatively sparse. Esters are usually characterized by hydrolysis, followed by separation—frequently tedious—and identification of the acid and alcohol portions, or they may be converted directly to certain derivatives (hydroxamic acids, amides, etc.) which permit identification of the acid moiety. In either case, the ester is destroyed and, of course, nonrecoverable.

The preparation of urea complexes of long-chain fatty acids, esters, and alcohols has already been reported (1, 8-10, 21), although techniques for obtaining the complexes in high yields (75 to 100%) have not been adequately described. Urea complexes meet almost all the criteria for an ideal derivative. For example, urea complexes are well-defined, large, easily handled crystals; they are readily prepared in high yield (see Experimental); the "crude" complexes are substantially analytically pure without recrystallization; no special reagents or techniques are required for their preparation; the organic compound bound in the complex is readily recovered by addition of water to dissolve the urea; and the weight ratio of urea to organic compound is 3 to 1, thereby resulting in a significant increase in weight of material to be handled. In 42 urea complexes from long-chain acids, esters, and alcohols, this weight ratio appeared to be an invariant characteristic.

X-ray powder patterns of most urea complexes are identical but different from that of urea. Although x-ray powder patterns

cannot be used to identify specific complexes, such determinations are useful in confirming that a complex has been formed. Unfortunately, the melting point of all urea complexes reported thus far is that of urea, and consequently this property, also, cannot be employed for identification purposes. In determining the melting point of urea complexes by the capillary method, however, it is observed that before the melting point of urea is reached, there is an exudation of a small amount of liquid. The authors concluded, therefore, that at some temperature below the melting point of urea the complexes dissociate into their components, which in all cases so far studied are apparently immiscible, thus accounting for the exudation; the melting point is that of urea.

If an attempt is made to determine the melting point of a few transparent crystals of a urea complex, employing a hot stage attached to a low- or medium-power microscope, one observes that the crystals of most complexes become milky and opaque prior to any exudation of liquid. If the temperature is increased slowly, particularly just below the temperature at which opacity is first observed, the entire body of the crystals becomes milky and opaque over a narrow temperature range, usually 1°C . The temperature at which opacity occurs can be readily duplicated, usually within $\pm 1.5^\circ$. At this characteristic temperature, the complex dissociates and the transparent, hexagonal crystals are converted to an aggregate of tetragonal microcrystals, but retain their original external form. This temperature is called the dissociation temperature of a urea complex; it is the temperature at which opacity first occurs when a transparent crystal of a urea complex is slowly heated. This dissociation temperature is not that reported by Redlich *et al.* (8), who determined the maximum stability of the complex in contact with an aqueous solution of urea.

In this paper, a technique is reported for the preparation in high yield (75 to 100%) of urea complexes from 42 long-chain compounds, consisting of fatty acids, methyl and vinyl esters, alcohols, a mono- and diglyceride, and a vinyl ether. These include

Table I. Composition of Urea Complexes^a

Acids	Ratio of Urea to Acid ^b		Methyl Esters	Ratio of Urea to Ester ^c		Alcohols	Ratio of Urea to Alcohol ^d		Misc. Compounds	Ratio of Urea to Compound ^e	
	Molar	Weight		Molar	Weight		Molar	Weight		Molar	Weight
Caprylic ^f	6.7	2.8	Caprylate ^f	6.7	3.3	Octanol (10)	6.9	3.2	Vinyl pelargonate ^f	10.2	3.3
Pelargonic ^f	7.4	2.8	Vinyl palmitate ^f	15.1	3.2
Capric ^f	8.0	2.8	Caprate ^f	9.6	3.1	Vinyl octadecyl ether ^g	13.9	2.8
Lauric ^f	9.7	2.9	Laurate ^f	11.1	3.1	Dodecanol ^h	9.6	3.1	1-Monopalmitin ^g	17.1	3.1
Tridecyl ^g	11.8	3.3
Myristic ^f	10.6	2.8	Myristate ^f	12.1	3.0	Tetradecanol ^h	11.1	3.1
Palmitic ^f	12.0	2.8	Palmitate ^f	13.5	3.0	Hexadecanol ^h	12.1	3.0
Stearic ^g	14.7	3.1	Stearate ^g	14.4	2.9	Octadecanol ^h	13.5	3.0
Oleic (cis) ^f	13.6	2.9	Oleate (cis) ^f	14.3	2.9	Oleyl (cis) ^h	14.3	3.2
Elaidic (trans) ^f	13.6	2.9	Elaidate (trans) ^f	13.9	2.8	Elaidyl (trans) ^h	14.3	3.2
10-Hendecenoic ^h	9.2	3.0
9,10-Epoxy stearic ^f , m.p. 59°	13.4	2.7
9,10-Epoxy stearic ^f , m.p. 55°	13.4	2.7
9,10-Dihydroxystearic ^h , m.p. 95°	14.7	2.8	9,10-Dihydroxystearate ^h , m.p. 70°	14.9	2.7
12-Hydroxystearic ^h	14.0	2.8	9,10-Dihydroxystearate ^h , m.p. 103°	14.9	2.7
12-Ketostearic ^h	14.4	2.9

^a "Recrystallized" from methanol or methanol-isopropyl alcohol, one half to two thirds saturated with urea.

^b Calculated from acid number of complex.

^c Calculated from saponification number of complex, corrected for interference by urea (saponification No. 1-2).

^d Calculated from per cent nitrogen of complex.

^e Calculated from iodine number or saponification number of complex.

^f Complex prepared by Technique 1.

^g Complex prepared by Technique 2.

^h Complex prepared by Technique 2, except that 80:20 methanol-isopropyl alcohol was employed as solvent.

several cis-trans pairs and some long-chain compounds with oxygen-containing functional groups in the chain. The dissociation temperature of most of these urea complexes has been determined, and use of this new characteristic for identification purposes is discussed.

EXPERIMENTAL

Materials Used. Urea was reagent grade; absolute methanol was ACS reagent grade. Procedures have already been reported for the preparation of pure caproic (14), caprylic (14), pelargonic (14), capric (14), lauric (14), myristic (14), palmitic (14), stearic (14), oleic (2, 16, 19), elaidic (17), 10-hendecenoic (undecylenic) (5), 12-ketostearic (6), cis-9,10-epoxystearic (4), trans-9,10-epoxystearic (4), and low-melting 9,10-dihydroxystearic acids (12), methyl caprylate (14), caprate (14), laurate (14), myristate (14), palmitate (14), stearate (14), oleate (17), elaidate (17), and low- and high-melting 9,10-dihydroxystearates (13), vinyl pelargonate (14), laurate (14), palmitate (14), and stearate (14), oleyl (16), elaidyl (15), dodecyl (lauryl) (13), tetradecyl (myristyl) (13), hexadecyl (cetyl) (13), and octadecyl (stearyl) (13) alcohols.

12-Hydroxystearic acid, melting point 81°, was prepared from the mixed fatty acids of completely hydrogenated castor oil by extraction of solubles (saturated, nonhydroxylated fatty acids) in a Soxhlet extractor with commercial hexane, followed by recrystallization of the insoluble portion (crude 12-hydroxystearic acid) from acetone. Tridecyl acid was Eastman Kodak white-label grade. Mono- and dipalmitin were obtained from B. F. Daubert, formerly of the University of Pittsburgh, and vinyl octadecyl ether was obtained from General Aniline and Film Corp. *n*-Nonanol was obtained from C. O. Badgett of this laboratory and was fractionally distilled before use.

Preparation of Urea Complexes. Two general techniques were developed. The first (Technique 1) is recommended for exploratory purposes and if the yield of complex is of secondary importance; the "crude" complex, however, is pure and recrystallization is unnecessary. The second (Technique 2) gives high yields of complex (75 to 100%) and, in most cases, the "crude" complex is pure without recrystallization.

TECHNIQUE 1. One gram of organic compound is dissolved in 20 ml. of absolute methanol containing 3 grams of urea; if necessary, heat is used. (If the compound does not dissolve completely, isopropyl alcohol is added dropwise to the hot solution until homogeneity is attained.) The solution is allowed to stand at room temperature (22° to 28°) for several hours (or overnight, if desired), and the long, needlelike crystals of complex are then

filtered by suction. All the compounds described in this paper can be handled as just described, but with volatile compounds suction filtration may cause evaporation of the organic compound. The filtrate may be cooled to 0° to 10° if an additional yield of complex is desired or if no precipitate is obtained at room temperature.

A blank experiment in which 1 gram of organic compound is dissolved in 20 ml. of methanol or methanol-isopropyl alcohol (urea absent) should also be run. Absence of precipitation in the blank but precipitation in the other is usually positive evidence that the organic compound forms a urea complex.

TECHNIQUE 2. If it is known from fundamental considerations (1, 8-10, 21) or if it has been shown by Technique 1 that the compound to be treated will form a urea complex, Technique 2 is recommended. In this technique, the ratio of organic compound to urea to solvent is 1:4-6:7-20. For the majority of substances, high yields of pure complex are obtained directly when the ratio is 1:5:20, and quantitative yields are frequently obtained when the ratio is 1:5:7, although in the latter instance some urea contamination of complex may also occur.

"Recrystallization" of Urea Complexes. Urea complexes may be recrystallized from methanol or isopropyl alcohol in recoveries usually not exceeding 60%, or from the same solvents one half or two thirds saturated with urea in recoveries ranging from 60 to 100%. A urea complex is considered pure when recrystallization does not change its composition, as determined by the analytical methods briefly described below.

Analysis of Urea Complexes. The composition of complexes of fatty acids or esters is calculated from the acid or saponification number, respectively, of the complex. Urea has a small saponification number (1 to 2), for which a correction must be made. Complexes of unsaturated compounds are analyzed by determination of the iodine number of the complex. When functional group methods are unavailable or inapplicable, ultimate analysis (C, H, N, etc.) can be used. In several instances in which both types of analysis were employed as a cross check on composition, the results agreed well. Table I lists both the molar and weight composition of the majority of the urea complexes prepared during this investigation. The weight ratio of urea to organic compound is 3.0 (±0.3) to 1 in all the complexes reported in this paper (Table I).

Dissociation Temperatures of Urea Complexes. The dissociation temperatures of the urea complexes were determined at atmospheric pressure on recrystallized complexes with a Koffler

micro hot stage attached to a conventional microscope. The Kofler micro hot stage with the necessary accessories (heat baffle, circular cover glass with ground-glass edge, cooling plate, etc.) may be purchased from laboratory supply houses. Complete instructions for its use are furnished with the apparatus. The magnification employed was usually 24 to 40 \times , depending on the size of the crystals. The conventional Kofler technique for determining melting points was employed, except that the crystals of complex (usually 2 to 5) were placed on a polished copper strip approximately $\frac{1}{2} \times \frac{3}{4} \times \frac{1}{32}$ inch instead of on a cover glass or microscope slide. The source of light was a microscope illuminator containing an ordinary tungsten lamp. The temperature was raised at a rate not exceeding 1° in 5 minutes within 5° of the dissociation temperature (determined approximately by rapid heating in a trial run), and the determination was stopped when a definite milkiness could be observed in the transparent crystals. If the heating was continued beyond the dissociation temperature, the melting point of urea was ultimately reached, at which point the typical melting phenomenon was observed.

Several crystals of urea complex were placed within the field of vision during the determination, so that duplicate values of the dissociation temperature could be obtained in a single run. These values usually agreed within $\pm 1.5^\circ \text{C}$.

Figure 1 is a photomicrograph made with transmitted light of A, an undissociated urea-methyl oleate complex, B, the complex at its dissociation temperature (110°), and C, the completely dissociated complex. Occasionally, at or a little above the dissociation temperature, a urea complex disintegrates, as shown in Figure 1, C, second crystal from the left. Observed microscopically, this is a spectacular illustration of the dissociation of a urea complex.

It is imperative to select transparent, well-formed crystals to obtain concordant results. When isopropyl alcohol or methyl ethyl ketone is employed in the preparation of the complexes, nontransparent crystals are usually obtained. These are generally unsuitable for determination of dissociation temperatures by this technique.

When the dissociation temperature exceeds about 110°, sublimation of urea fogs the heat baffle, and it is necessary to reach under the circular cover glass with a pair of long tweezers (or other suitable tool) and quickly move the heat baffle slightly so that the crystals remain visible throughout.

RESULTS AND DISCUSSION

Table II lists the dissociation temperatures of the urea complexes studied. It is evident that the dissociation temperatures of the complexes from each homologous series are sufficiently far

apart to permit the use of this characteristic for identification purposes. Furthermore, the dissociation temperature increases uniformly with increasing chain length in each homologous series instead of exhibiting the alternation phenomenon so frequently encountered among aliphatic compounds. With compounds whose dissociation temperatures are approximately 75° or lower, it is recommended that the determination be carried out as soon as possible after the preparation of the complex. Otherwise, some evaporation may occur, and the crystals of complex, instead of being transparent, may have an over-all surface cloudiness which interferes with the determination.

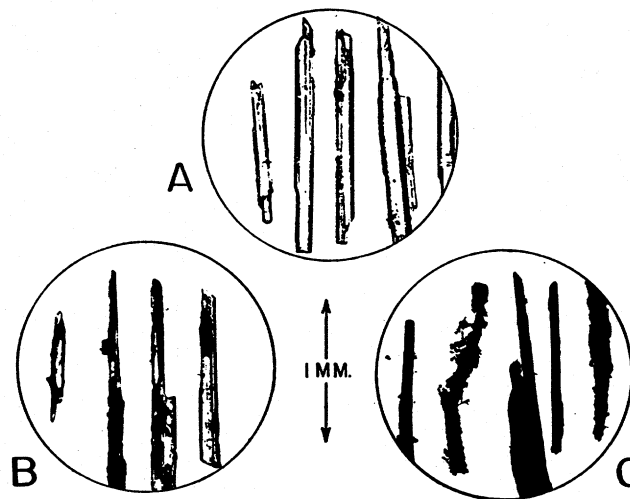


Figure 1. Dissociation of Urea-Methyl Oleate Complex

- A. Undissociated complex
B. Complex at dissociation temperature (110°)
C. Completely dissociated complex

In the saturated fatty acid series (Table II), the difference in dissociation temperature between the urea complexes of caproic (C_6) and stearic (C_{18}) acids is about 60°, and the difference between the dissociation temperatures of the urea complexes of lauric (C_{12}) and stearic acids is about 33°. For identification purposes, the latter difference is of great utility because the melting

Table II. Dissociation Temperatures^a of Urea Complexes

Acids	Dissociation Temp., °C.	Methyl Esters	Dissociation Temp., °C.	Alcohols	Dissociation Temp., °C.	Misc. Compounds	Dissociation Temp., °C.
Caproic	64 ^b	Vinyl pelargonate	52
Caprylic	73	Caprylate	55	Vinyl laurate	79
Pelargonic	80.5	Nonanol	57	Vinyl palmitate	113
Capric	85	Caprate	67	Decanol	68	Vinyl stearate	c
Lauric	92.5	Laurate	77.5	Dodecanol	80	Vinyl octadecyl ether	125.5
Tridecyl	96	1-Monopalmitin	c
Myristic	103	Myristate	96	Tetradecanol	91	1,3-Dipalmitin	c
Palmitic	114	Palmitate	118	Hexadecanol	107		
Stearic	126	Stearate	132 ^d	Octadecanol	124		
Oleic (<i>cis</i>)	110	Oleate (<i>cis</i>)	110	Oleyl (<i>cis</i>)	98		
Elaidic (<i>trans</i>)	116	Elaidate (<i>trans</i>)	125	Elaidyl (<i>trans</i>)	118		
10-Hendecenoic	90		
9,10-Epoxy stearic, m.p. 59° (<i>cis</i>)	118		
9,10-Epoxy stearic, m.p. 55° (<i>trans</i>)	125		
9,10-Dihydroxy stearic, m.p. 95°	107	9,10-Dihydroxy stearate, m.p. 70°	120		
12-Hydroxy stearic, m.p. 81°	125	9,10-Dihydroxy stearate, m.p. 103°	114		
12-Ketostearic, m.p. 81.5°	115		

^a Average of at least three determinations. Same average values for dissociation temperatures were obtained whether crystals came from same preparation or different ones.

^b Pure caproic acid-urea complex could not be obtained. Dissociation temperature reported is point at which opacity was first observed, but entire body of crystals did not become opaque, even though determination was conducted up to melting point of urea (133°).

^c Crystals of undissociated complex were opaque, and therefore, technique could not be employed.

^d In this case, it was difficult to observe whether dissociation occurred just before crystals melted. This value may not be reliable, although there is no doubt that dissociation temperature is at least 130°.

points of the commonly used derivatives of C_{12} to C_{18} fatty acids are usually close together. The spread in dissociation temperatures observed in the methyl ester series is about 75° ; in the alcohol series, 70° ; and in the vinyl ester series, 60° (Table II).

Another advantage in employing urea complexes for identification purposes is the ease with which the organic compound bound with urea can be recovered. Addition of water to the complex dissolves the urea and leaves the organic compound as an immiscible liquid or solid, which can be employed in the preparation of an additional derivative. In the identification of esters, this feature is of considerable value because most other techniques for identifying esters with which the authors are familiar involve destruction of the compound.

Furthermore, the technique is readily applicable on a semi-micro or micro scale, as only a few crystals are required and the weight of complex usually obtained when Technique 2 is employed is three or four times the original weight of the organic compound. The physical character of the crystals and their ease of manipulation and drying are ideal.

Each homologous series (Figure 2) shows a linear relationship between dissociation temperature and total number of carbon atoms. This relationship is not unexpected from the structure of the complexes (10), which shows that urea associates in the presence of an aliphatic organic compound to form the walls of a narrow hollow hexagonal cylinder in which the organic component is held by secondary valence forces. The amount of energy required to break this association should, therefore, depend on chain length, with the van der Waals forces increasing regularly with each addition of a methylene group.

In addition, the association should be dependent on the number and position of the functional groups of the organic component. For example, the fatty acids should have an additional association force through hydrogen bonding involving the carboxyl end group. The reduction of the energy of association in going from acids to alcohols to esters is reflected in lower dissociation temperatures, and accounts for the relative position of the curves in Figure 2.

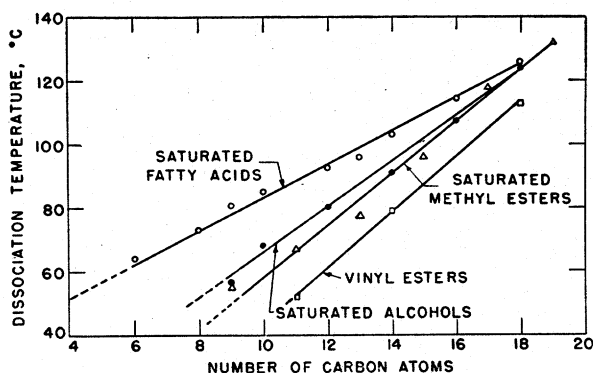


Figure 2. Dissociation Temperatures of Urea Complexes (Table II) Plotted against Number of Carbon Atoms in Organic Compounds

The curves for the four homologous series appear to converge between 130° and 140°C ., suggesting that the limiting value for dissociation temperature is the melting point of urea. This point is being checked by a study of the dissociation temperatures of C_{22} to C_{28} straight-chain compounds.

The decrease in the difference between the homologous series as the chain length increases is probably due to the fact that the stability of the complex is affected more by the association of the methylene groups than of the polar groups with urea.

Another point of theoretical interest is a comparison of the dissociation temperatures of the urea complexes of C_{18} cis-trans

isomers (oleic acid-elaidic acid, methyl oleate-methyl elaidate, oleyl alcohol-elaidyl alcohol). In each case, the dissociation temperature of the trans isomer is significantly higher than that of the cis isomer, although the secondary valence forces involved in the formation of complexes from these cis-trans pairs are identical. Examination of molecular models of cis-trans isomers shows that the trans isomers have little or no additional spatial requirements in the urea channel over those of the corresponding saturated compounds (cross section, about 4.1 Å.). On the other hand, the cis compounds have slightly greater spatial requirements, and slight distortion of the normal shape of the long-chain molecule must occur for them to fit within the spiral channel of urea. Thus, with the cis compounds some steric strain is present, and the complexes would be less stable than those from the corresponding trans isomers. The situation is reflected in lower dissociation temperatures of the urea complexes prepared from cis isomers.

The presence of oxirane, keto, or hydroxyl groups along the aliphatic chain does not prevent the ready formation of urea complexes (Table II) with the exception of that from high-melting 9,10-dihydroxystearic acid, melting point 131°C . This last observation and its use in assigning the correct spatial position to the hydroxyl groups in the isomeric 9,10-dihydroxystearic acids have already been reported (18).

As a result of this investigation, the following new classes of organic compounds have been shown to form urea complexes: vinyl esters, vinyl ethers, mono- and diglycerides, α -glycols, and oxiranes (Table II).

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